

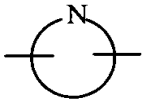
wherein R<sup>1</sup> is a substituted or unsubstituted N-containing cycloalkyl,

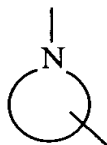
R<sup>2</sup> is carboxy or protected carboxy,


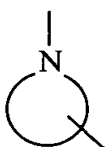
A<sup>1</sup> is a substituted or unsubstituted lower alkylene, a substituted or unsubstituted lower alkanyl-ylidene or a substituted or unsubstituted lower alkenylene,

A<sup>2</sup> is lower alkylene,

A<sup>3</sup> is a substituted or unsubstituted lower alkylene,

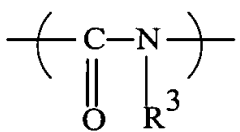
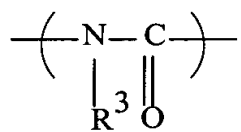
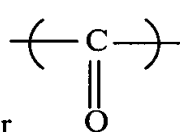
 is a group of the formula:



 wherein  is a substituted or unsubstituted N-containing heterocyclic group,

X is O, S or NH,

Y is NH,

Z is ,  or 

wherein R<sup>3</sup> is hydrogen or lower alkyl,

ℓ, m and n are each the same or a different integer of 0 or 1,

and a pharmaceutically acceptable salt thereof.

2. (Amended) The compound of claim 1,

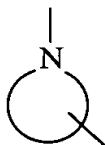
wherein R<sup>1</sup> is a substituted or unsubstituted 3 to 8 membered cycloalkyl containing 1 to 3 nitrogen atom(s),

R<sup>2</sup> is a carboxy or an esterified carboxy,

A<sup>1</sup> is a substituted or unsubstituted lower alkylene, a substituted or unsubstituted lower alkanyl-ylidene or a substituted or unsubstituted lower alkenylene,

A<sup>2</sup> is lower alkylene,

A<sup>3</sup> is a substituted or unsubstituted lower alkylene,

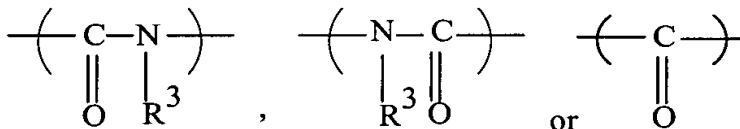


is a substituted or unsubstituted saturated 3 to 8 membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), a substituted or unsubstituted unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s) or a substituted or unsubstituted saturated 3 to 8-membered heteromonocyclic group containing 1 to 5 carbon atom(s), 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s),

X is O, S, or NH,

Y is NH,

Z is



wherein R<sup>3</sup> is hydrogen or lower alkyl;

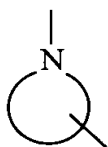
ℓ is an integer of 0 or 1,

m is an integer of 0 or 1,

n is an integer of 0 or 1.

3. (Amended) The compound of claim 2,

wherein R<sup>1</sup> is an unsubstituted piperidyl or a substituted piperidyl containing 1 or 2 oxo or [5-(lower) alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl,



is piperidyl, morpholinyl, tetrahydroquinolyl or pyrrolidinyl,

A<sup>3</sup> is an unsubstituted lower alkylene or a substituted lower alkylene containing 1 to 3 suitable substituent(s) selected from the group consisting of (C<sub>1</sub>-C<sub>6</sub>)alkyl; (C<sub>2</sub>-C<sub>6</sub>)alkenyl; (C<sub>2</sub>-C<sub>6</sub>)alkynyl; phenyl; phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl; phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl having 1 to 4 (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halo (C<sub>1</sub>-C<sub>6</sub>) alkyl or (C<sub>1</sub>-C<sub>6</sub>)alkylene dioxy; (C<sub>1</sub>-C<sub>6</sub>)alkyl having unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s); cyano; amino; protected amino; and phenyl(C<sub>1</sub>-C<sub>6</sub>)alkylcarbamoyl;

R<sup>2</sup>, R<sup>3</sup>, A<sup>1</sup>, A<sup>2</sup>, X, Y or Z are each as defined in claim 2,

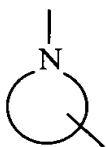
ℓ is an integer of 0,

m is an integer of 0,

n is an integer of 0.

4. (Amended) The compound of claim 3,

wherein R<sup>1</sup> is an unsubstituted piperidyl or a substituted piperidyl containing 1 or 2 oxo or [5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl,



is piperidyl, morpholinyl, tetrahydroquinolyl or pyrrolydinyl,

A<sup>3</sup> is an unsubstituted lower alkylene or a substituted lower alkylene containing 1 to 3 suitable substituent(s) selected from the group consisting of (C<sub>1</sub>-C<sub>6</sub>)alkyl; (C<sub>2</sub>-C<sub>6</sub>)alkenyl; (C<sub>2</sub>-C<sub>6</sub>)alkynyl; phenyl; phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl; phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl having 1 to 4 (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl or (C<sub>1</sub>-C<sub>6</sub>)alkylene dioxy; (C<sub>1</sub>-C<sub>6</sub>)alkyl having unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s); cyano; amino; (C<sub>1</sub>-C<sub>6</sub>)alkanoylamino; aroylamino which may have 1 to 3 hydroxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halogen or phenyl; cyclo(C<sub>3</sub>-C<sub>6</sub>)alkylcarbonylamino; (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkylcarbonylamino; (C<sub>2</sub>-C<sub>6</sub>)carbonylamino; (C<sub>1</sub>-C<sub>6</sub>)alkylsulfonylamino; phenylsulfonylamino; and phenyl(C<sub>1</sub>-C<sub>6</sub>)alkylcarbamoyl;

$R^2, R^3, A^1, A^2, X, Y$  or  $Z$  are each as defined in claim 3,

$\ell$  is an integer of 0,

$m$  is an integer of 0,

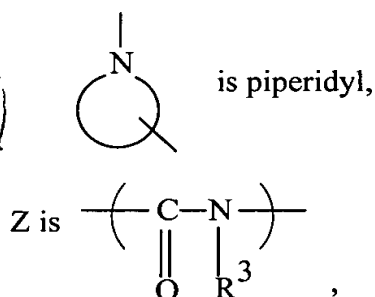
$n$  is an integer of 0.

5. (Amended) The compound of claim 4,

wherein  $R^1$  is piperidyl,

$A^1$  is a lower alkylene or a lower alkanyl-ylidene,

$A^3$  is an unsubstituted lower alkylene or a substituted lower alkylene containing a lower alkyl, a lower alkynyl or a lower alkanoylamino,



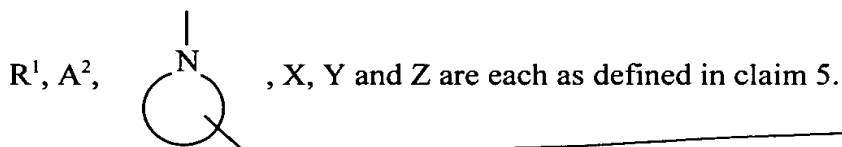
$R^2, R^3, A^2, Y, \ell, m,$  and  $n$  are each as defined in claim 4.

6. (Amended) The compound of claim 5,

wherein  $R^3$  is hydrogen,

$A^1$  is a lower alkylene,

$A^3$  is a lower alkylene having a lower alkanoylamino,

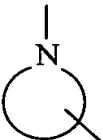


8. (Amended) The compound of claim 5,

wherein  $R^3$  is hydrogen,

B2  
1804  
 $A^1$  is a lower alkylene,

$A^3$  is a lower alkylene having a lower alkynyl,

$R^1, R^2, A^2,$  ,  $X, Y, Z, \ell, m$  and  $n$  are each as defined in claim 5.

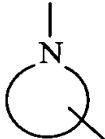
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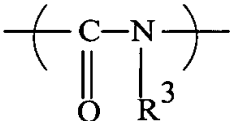
10. (Amended) The compound of claim 4,

wherein  $R^1$  is piperidyl,

$A^1$  is a lower alkylene or a lower alkanylylidene,

$A^3$  is an unsubstituted lower alkylene or a substituted lower alkylene containing a lower alkyl, a lower alkynyl or a lower alkanoylamino,

 is morpholinyl,

B3  
 $Z$  is ,

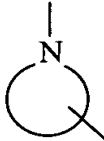
$R^2, R^3, A^2, Y, \ell, m$  and  $n$  are each as defined in claim 4.

11. (Amended) The compound of claim 5,

wherein  $R^3$  is hydrogen.

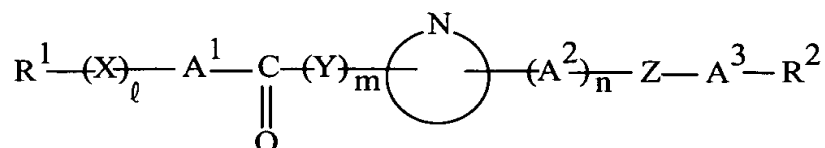
$A^1$  is a lower alkylene,

$A^3$  is a lower alkylene,

$R^1, A^2,$  ,  $X, Y$  and  $Z$ , are each as defined in claim 10.

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13. (Amended) A process for preparing a compound of the formula:



wherein  $R^1$  is a substituted or unsubstituted N-containing cycloalkyl,

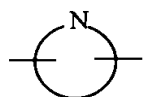
$R^2$  is a carboxy or a protected carboxy,

$A^1$  is a substituted or unsubstituted lower alkylene, a substituted or unsubstituted lower alkanyl-ylidene or a substituted or unsubstituted lower alkenylene,

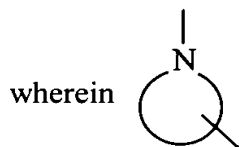
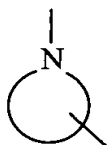
$A^2$  is a lower alkylene,

$A^3$  is a substituted or unsubstituted lower alkylene,

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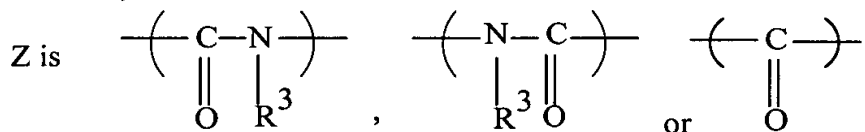
is a group of the formula:



wherein is a substituted or unsubstituted N-containing heterocyclic group,

$X$  is O, S or NH,

$Y$  is NH,

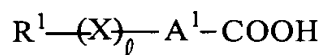


(wherein  $R^3$  is hydrogen or lower alkyl),

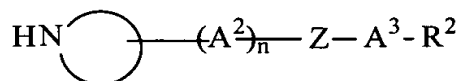
$\ell$ ,  $m$  and  $n$  are each the same or a different integer of 0 or 1,

and a salt thereof, which comprises

(i) reacting a compound of the formula

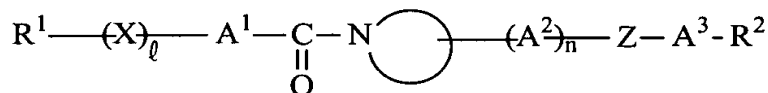


wherein  $R^1$ ,  $A^1$ ,  $X$  and  $\ell$  are each as defined above, or its reactive derivative at the carboxy group or a salt thereof, with a compound of the formula:



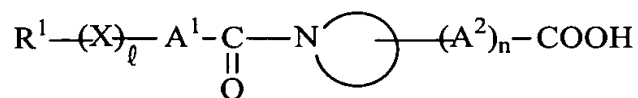
wherein  $R^2$ ,  $A^2$ ,  $A^3$ ,  $HN \bigcirc$ ,  $Z$  and  $n$  are each as defined above,

or its reactive derivative at the amino group or a salt thereof, to give a compound of the formula:



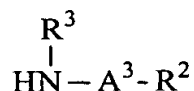
wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $-N \bigcirc$ ,  $X$ ,  $Z$ ,  $\ell$  and  $n$  are each as defined above, or a salt thereof, or

(ii) reacting a compound of the formula:

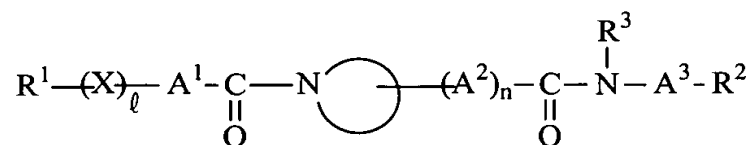


wherein  $R^1$ ,  $A^1$ ,  $A^2$ ,  $-N \bigcirc$ ,  $X$ ,  $\ell$  and  $n$  are each as defined above, or its reactive derivative at the carboxy group

or a salt thereof, with a compound of the formula:

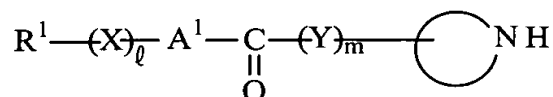


wherein  $R^2$ ,  $R^3$  and  $A^3$  are each as defined above, or its reactive derivative at the amino group or a salt thereof, to give a compound of the formula:

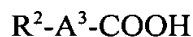


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $-\text{N}\bigcirc-$ ,  $X$ ,  $\ell$  and  $n$  are each as defined above, or a salt thereof, or

(iii) reacting a compound of the formula:

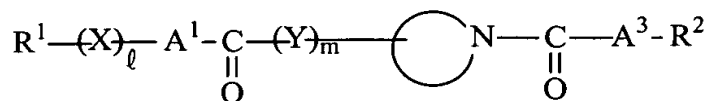


wherein  $R^1$ ,  $A^1$ ,  $\text{HN}\bigcirc-$ ,  $X$ ,  $Y$ ,  $\ell$  and  $m$  are each as defined above, or its reactive derivative at the amino group or a salt thereof, with a compound of the formula



wherein  $R^2$  and  $A^3$  are each as defined above,

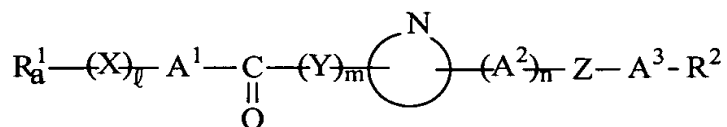
or its reactive derivative at the carboxy group or a salt thereof, to give a compound of the formula:



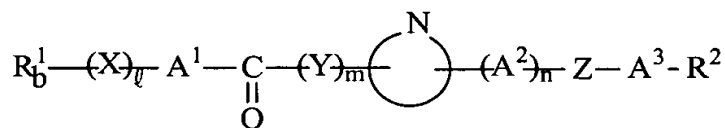
wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^3$ ,  $-\text{N}\bigcirc-$ ,  $X$ ,  $Y$ ,  $Q$  and  $m$  are each as defined above, or a salt thereof, or

(iv) subjecting a compound of the formula:



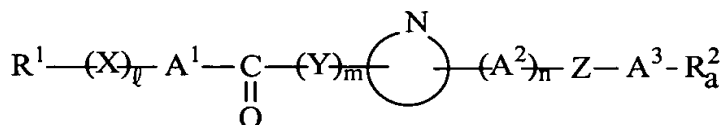


wherein  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and  $R_a^1$  is a substituted or unsubstituted N-containing cycloalkyl having amino protective group, or a salt thereof, to elimination reaction of the amino protective group, to give a compound of the formula:

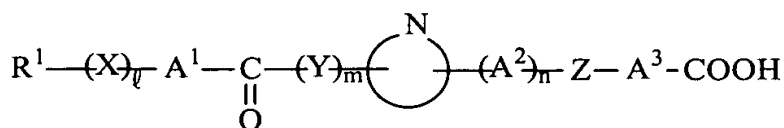


wherein  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and  $R_b^1$  is a substituted or unsubstituted N-containing cycloalkyl, or a salt thereof, or

(v) subjecting a compound of the formula:

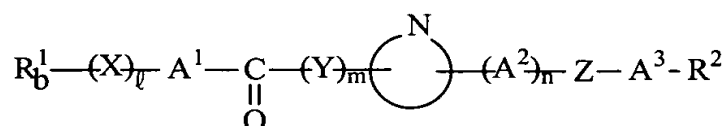


wherein  $R^1$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and  $R_a^2$  is protected carboxy, or a salt thereof, to elimination reaction of carboxy protective group, to give a compound of the formula:



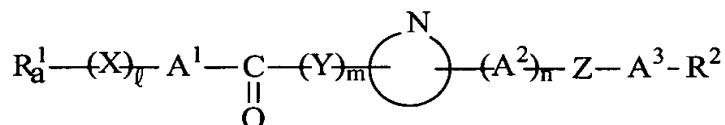
wherein  $R^1, A^1, A^2, A^3, \text{---}\text{N}\text{---}$ , X, Y, Z,  $\ell$ , m and n are each as defined above, or a salt thereof, or

(vi) subjecting a compound of the formula:



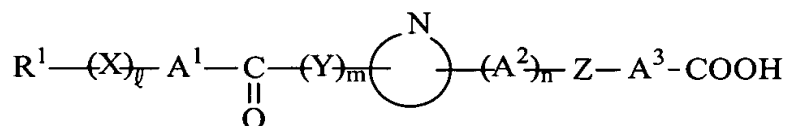
wherein  $R^2, A^1, A^2, A^3, \text{---}\text{N}\text{---}$ , X, Y, Z,  $\ell$ , m and n are each as defined above, and  $R_b^1$  is a substituted or unsubstituted N-containing cycloalkyl,

or a salt thereof, to protecting reaction of amino, to give a compound of the formula:

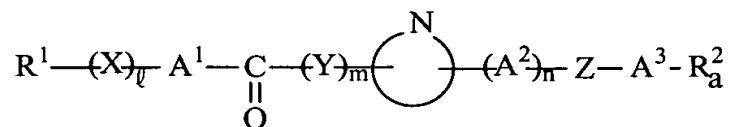


wherein  $R^2, A^1, A^2, A^3, \text{---}\text{N}\text{---}$ , X, Y, Z,  $\ell$ , m and n are each as defined above, and  $R_a^1$  is a substituted or unsubstituted N-containing cycloalkyl having amino protecting group, or a salt thereof, or

(vii) subjecting a compound of the formula:

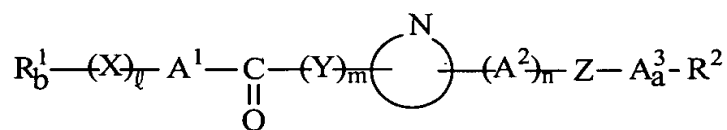


wherein  $R^1, A^1, A^2, A^3, \text{---}\text{N}\text{---}$ , X, Y, Z,  $\ell$ , m and n are each as defined above, or its reactive derivative at the carboxy group or a salt thereof, to protecting reaction of the carboxy, to give a compound of the formula:



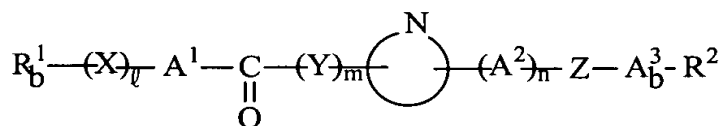
wherein  $R^1$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and  $R_a^2$  is a protected carboxy, or a salt thereof, or

(viii) subjecting a compound of the formula:



wherein  $R_b^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and

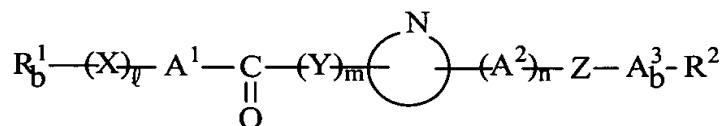
$A_a^3$  is lower alkylene having protected amino or a salt thereof, to elimination reaction of amino protective group, to give a compound of the formula:



wherein  $R_b^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and

$A_b^3$  is a lower alkylene having an amino or a salt thereof, or

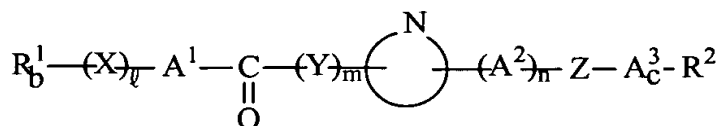
(ix) subjecting a compound of the formula:



wherein  $R_b^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and

$A_b^3$  is lower alkylene having amino, or a salt thereof, to acylation reaction of amino, to

give a compound of formula:



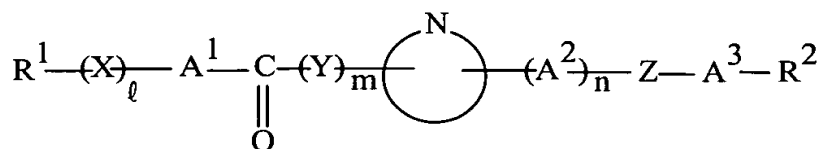
wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are each as defined above, and  $A^3$  is lower alkylene having acylamino, or a salt thereof.

16. (Amended) The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein said compound or pharmaceutically acceptable salt thereof is admixed with a pharmaceutically suitable carrier.

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17. (Amended) A method for the treatment of diseases caused by thrombus formation; restenosis or reocclusion; the thrombus formation in case of vascular surgery, valve replacement, extracorporeal circulation or transplantation; disseminated intravascular coagulation; thrombotic thrombocytopenic; essential thrombocytosis; inflammation; or for the adjuvant therapy with thrombolytic drug or anticoagulant; which comprises administering a compound of claim 1 or a pharmaceutically acceptable salt thereof to a human being or an animal.

18. (Amended) A compound of the formula:



wherein:

$R^1$  is a 6-membered cyclo(lower)alkyl containing 1 to 3 nitrogen atoms which may have one or more amino protective groups;

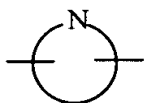
$X$  is O, S or NH, and

$\ell$  is an integer of either 0 or 1;

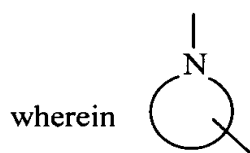
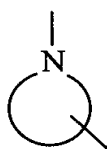
$A^1$  is a substituted or unsubstituted lower alkylene, a substituted or unsubstituted lower alkenylene or a substituted or unsubstituted lower alkanyl-ylidene;

$Y$  is  $NH$ , and

$m$  is an integer of either 0 or 1;

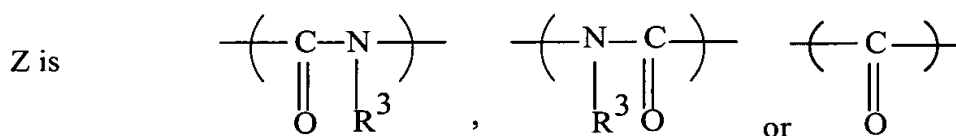


is a group of the formula:



wherein is a substituted or unsubstituted 5 or 6-membered N-containing heterocyclic group containing 1 to 3 nitrogen atoms;

$A^2$  is a lower alkylene, and  $n$  is an integer of either 0 or 1;



wherein  $R^3$  is hydrogen or a lower alkyl;

$A^3$  is a substituted or unsubstituted lower alkylene;

and  $R^2$  is a carboxy or a protected carboxy;

or a pharmaceutically acceptable salt thereof.

Please add the following new claims:

22. (New) A method of producing a medicament, comprising mixing the compound of claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically suitable carrier.

23. (New) A method for the treatment of a disease caused by thrombus formation comprising administering to a patient in need thereof an effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof .

24. (New) The method of claim 23, wherein said disease caused by thrombus formation is restenosis or reocclusion; the thrombus formation in case of vascular surgery, valve replacement, extracorporeal circulation or transplantation; disseminated intravascular coagulation; thrombotic thrombocytopenic; essential thrombocytosis; or inflammation.

25. (New) The compound of claim 16, wherein said compound is N-[(R)-1-{3-(4-piperidyl)propionyl}-3-piperidylcarbonyl]-β-alanine hydrochloride.

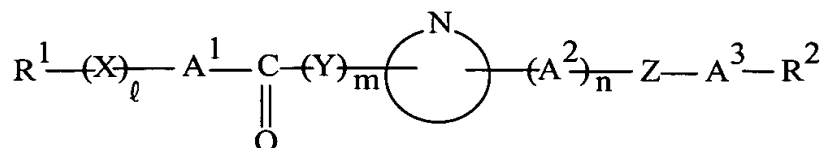
26. (New) The method of claim 17, wherein said compound is N-[(R)-1-{3-(4-piperidyl)propionyl}-3-piperidylcarbonyl]-β-alanine hydrochloride.

27. (New) The method of claim 22, wherein said compound is N-[(R)-1-{3-(4-piperidyl)propionyl}-3-piperidylcarbonyl]-β-alanine hydrochloride.

28. (New) The method of claim 23, wherein said compound is N-[(R)-1-{3-(4-piperidyl)propionyl}-3-piperidylcarbonyl]-β-alanine hydrochloride.

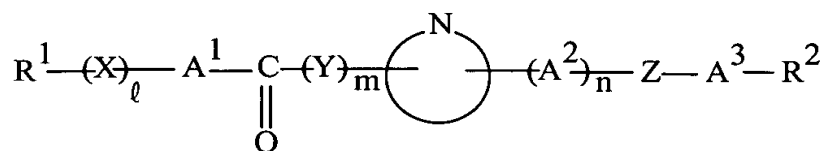
29. (New) N-[(R)-1-{3-(4-piperidyl)propionyl}-3-piperidylcarbonyl]-β-alanine or its hydrochloride.

30. (New) The process of claim 13 for preparing a compound of the formula:



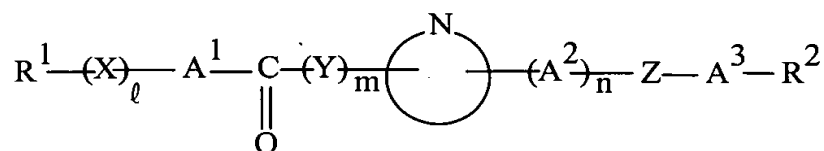
wherein  $R^1, R^2, A^1, A^2, A^3, \text{N}, X, Y, Z, \ell, m$  and  $n$  are as defined in claim 13,  
wherein said process comprises the process defined in section (i) of claim 13.

31. (New) The process of claim 13 for preparing a compound of the formula:



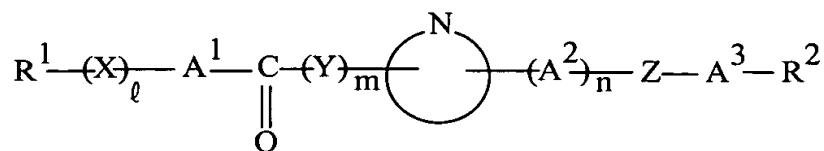
wherein  $R^1, R^2, A^1, A^2, A^3, \text{N}, X, Y, Z, \ell, m$  and  $n$  are as defined in claim 13,  
wherein said process comprises the process defined in section (ii) of claim 13.

32. (New) The process of claim 13 for preparing a compound of the formula:



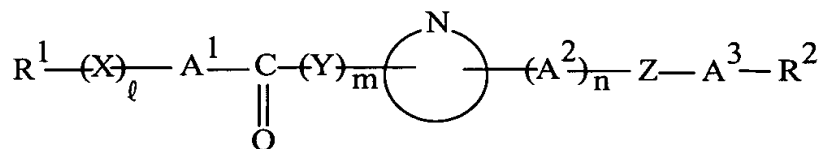
wherein  $R^1, R^2, A^1, A^2, A^3, \text{N}, X, Y, Z, \ell, m$  and  $n$  are as defined in claim 13,  
wherein said process comprises the process defined in section (iii) of claim 13.

33. (New) The process of claim 13 for preparing a compound of the formula:



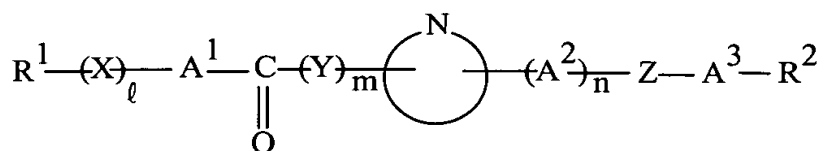
wherein  $R^1, R^2, A^1, A^2, A^3, \text{N}, X, Y, Z, \ell, m$  and  $n$  are as defined in claim 13,  
wherein said process comprises the process defined in section (iv) of claim 13.

34. (New) The process of claim 13 for preparing a compound of the formula:



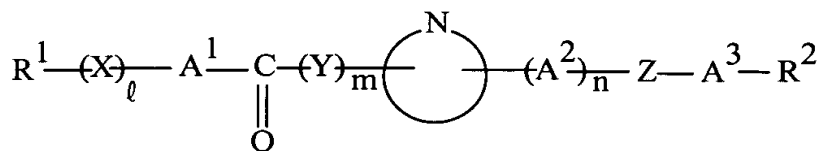
wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are as defined in claim 13, wherein said process comprises the process defined in section (v) of claim 13.

35. (New) The process of claim 13 for preparing a compound of the formula:



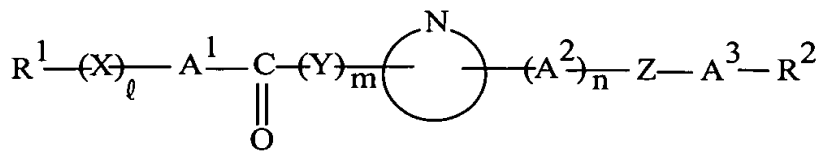
wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are as defined in claim 13, wherein said process comprises the process defined in section (vi) of claim 13.

36. (New) The process of claim 13 for preparing a compound of the formula:



wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are as defined in claim 13, wherein said process comprises the process defined in section (vii) of claim 13.

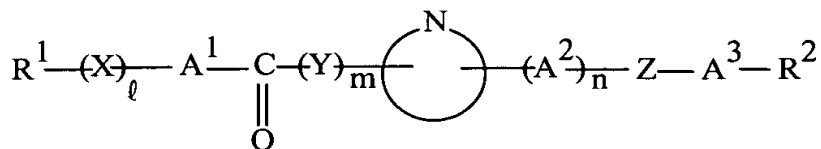
37. (New) The process of claim 13 for preparing a compound of the formula:



wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are as defined in claim 13, wherein said process comprises the process defined in section (viii) of claim 13.



38. (New) The process of claim 13 for preparing a compound of the formula:



wherein  $R^1$ ,  $R^2$ ,  $A^1$ ,  $A^2$ ,  $A^3$ ,  $\text{N}$ ,  $X$ ,  $Y$ ,  $Z$ ,  $\ell$ ,  $m$  and  $n$  are as defined in claim 13,

wherein said process comprises the process defined in section (ix) of claim 13.

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#### BASIS FOR THE AMENDMENT

Claim 15 has been canceled.

Claims 1-6, 8, 10, 11, 13, and 16-18 have been amended.

New Claims 22-38 have been added.

The amendment of Claims 1-6, 8, 10, 11, 13, and 16-18 is supported by original Claims 1-6, 8, 10, 11, 13, and 16-18. New Claims 22-24 are supported by page 1, line 21 to page 2, line 29. New Claims 25-29 are supported by Example 21(3) at page 125, line 34 to page 126, line 12. New Claims 30-38 are supported by page 4, line 21 to page 13, line 13.

No new matter is believed to have been added by these amendments.

#### REMARKS

Claims 1-14 and 16-38 are active in the present application.

Applicants wish to thank Examiner Robinson and Examiner Rotman for the helpful and courteous discussion with their undersigned Representative on February 20, 2002, and for the indication that Claim 21 is allowable.

The rejection of Claims 1-20 under 35 U.S.C. §112, first paragraph, is obviated in part by amendment and traversed in part.